"AUTO-INTOXICATION IN PREGNANCY."

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S C H E M E O F T H E S I S.

Introduction.

General doctrine of Auto-intoxication,

Special application to pregnancy.

Clinical illustrations. (twenty cases).

- Anaemia.
- Chorea.
- Peripheral Neuritis.
- Hyperemesis Gravidarum.
- Hepato-Toxaemia.
- Eclampsia.
- Acute Yellow Atrophy.
- Various minor symptoms.
- Mental disorders.

Therapeutic Indications.

To the student, approaching the subject from the standpoint of general biology, it is a matter for surprise that the process of reproduction in the human subject, in its three phases of pregnancy, parturition and puerpery, should so often be accompanied by abnormal manifestations; that a process essentially physiological should so often assume the pathological. Without dwelling on the mortality of child-birth or the graver difficulties of parturition, the fact becomes more and more evident that, apart from the mechanical disabilities of pregnancy, a very large proportion of gravid women suffer more or less seriously in health during that period. In complete accord with this, Playfair writes, "Making every allowance, therefore, for the undoubted fact that pregnancy ought to be a perfectly healthy condition, it must be conceded that in the vast majority of cases coming under our notice, it is not entirely so." And a few years experience of practice serves only to confirm the truth of the statement, and to impress on one the discomforts and dangers of the pregnant state, under the artificial conditions in which we live compared with those of the lower types of humanity, and more markedly still, compared with lower members in the scale of animal creation.

The pathology of pregnancy is for the purposes of description variously subdivided by different authors/

authors and teachers. Usually a division by systems is followed, e.g. Respiratory, Digestive etc. A convenient first division is into three main groups.

(1) Accidental diseases - with no causal relationship to pregnancy but which may modify or be modified by it, e.g. the specific fevers, cardiac diseases etc.

(2) Diseases due directly or indirectly to pregnancy.

(3) Morbid states of the uterus and ovum locally.

The first and third of these groups I set aside as foreign to my particular subject. The second of them can very well be subdivided further, on an etiological basis into

A. Those of mechanical origin.

B. Diseases of the nature of nervous reflexes

C. Manifestations of Autogenetic - toxaemia or "self-poisoning."

It is to this last group, which is increasing at the expense of that immediately preceding it, and which modern pathology is proving to be daily more comprehensive, that I wish to direct attention more particularly in the present thesis. The occurrence within a brief space of time of cases of chorea, anaemia, and eclampsia of pregnant women seen in the course of general practice has suggested the inquiry as/

as to how far such cases can be explained on a common basis. And if the doctrine of Auto-intoxication does not afford a final explanation of the ultimate causes, it affords a suitable working hypothesis as to the mode of action of such conditions and carries the inquiry a step further back, till, in short, further light is afforded by future research into the pathological chemistry of the cell. Further, it suggests and justifies in the field of Therapeutics certain measures which, as practitioners, we may take to anticipate and prevent their appearance or to antagonise and combat them when developed.

The doctrine of Auto-intoxication has its chief exponent in Bouchard and his followers, notably Charrin, Roger and Frenkel, of the French school of physiology - Bouchard's book "Les Auto-intoxications dans les Maladies," being the most systematic account of his researches and conclusions. The method of his research was what may be termed a physiological analysis of urine. The phenomena following intravenous injection of normal human urine into rabbits were noted and the relationship between the urinary toxicity and the body weight expressed in a numerical form, termed the "urotoxic coefficient." Thus a man weighing 60 kilos eliminates 1200 c.c. urine in 24 hours and if 50 c.c. of urine suffice to kill 1 kilo of living animal matter it follows that "on an average in/

in 2 days and 4 hours a man makes a mass of urinary poison capable of intoxicating himself" (1) And, "L'urotoxie" being defined as the quantity of toxic matter necessary to kill 1 kilo, the "co-efficient urotoxique" is the number or fraction of urotoxies formed in 24 hours per kilo of the individual. Proceeding from this fundamental determination he isolated the elements which in the urine produced the specifi specific phenomena observed in order. Frenkel(2) summarises the methods and results concisely.

> "Une analyse très minutieuse a montré que les substances qui fond rétrécir la pupille, à la manière de l'ésérine, peuvent être séparées de l'urine par le charbon animal que décolore l'urine; que les parties de l'urine insolubles dans l'alcool produisent le myosis, les convulsions, l'hyperthermie, tandis que l'extrait alcoolique provoque la somnolence, le coma, la salivation, que la diurése est due principalement à l'urée si abondante dans l'urine: que les substances convulsiveantes sont de deux ordres les unes minérales, comme la potasse, les autres organiques."

and again,

> "La conclusion la plus importante que se dégage de nombreuses études faites sur ce sujet est que/

que lorsque les fonctions rénales sont troublées, les toxines de l'organisme passent en bien moindre quantité dans l'urine qu'à l'état normal."

The importance of this with regard to the origin and early recognition of impending Eclampsia is self-evident, apart from its bearing on the wider problems of renal insufficiency and uraemia.

Too little is known at present with any definiteness as regards the internal secretion of the Kidney but the general trend of opinion seems to be to confirm the earlier results of Brown-Sequard that the action is anti-toxic[3] both generally - to neutralise substances injurious to the main functions of the organism, and locally - to prevent injury to the secreting cell - structure of the Kidney.

A large mass of continental experimental evidence bears out generally Bouchard's conclusions, but it is well to note that some have criticised his results adversely. Of these, the most recent, Herringham[4] in a paper read before the Pathological Society of London, maintains that, instead of all the elements contributing in varying proportions to the toxicity of urine, this toxicity is due almost entirely to potass alone.

As to the origin of these toxic substances, it is important/

important to differentiate their two sources. Ewald(5)in a comprehensive article dealing with the general aspects of the subject accompanied by a full bibliography emphasis this:-

"Die Quelle derartiger Producte kann nun so wohl innerhalb als ausserhalb der eigentlichen Zellterritorien des organismus liegen, d.h. sie kann intestinal (innerhalb des Verdauungstractes) oder interstitiell (innerhalb der Gewebe) ihren Ursprung nehmen."

Of the first group he cites as examples the headaches and giddiness of chronic dyspepsia, urticaria, pruritus and some anaemias; of the second, uraemia, gout, leukaemia, the cachexia of cancer, eclampsia and others. He points out also the necessity of recognising that the precursors, in the fluids and tissues, of effete substances which appear in the secretions are themselves toxic.

Thus he adds, "Zum anderen kommen die Producte des sog. intermediären Stoffwechsels in Betracht, also die zahlreichen Körper, welche durch reducirende oder oxydirende Processe, durch Hydration und Dehydration, sowie durch Synthesen entstehen, wie etc.

In brief, "Toxic substances are" to quote Farquharson(6)"necessary products of the normal discharge of cell functions/

functions, constantly formed in the cell and excreted in small quantities or developed in the materials in contact with the cell. Accumulation of these products in the body may arise in various ways, and when it does occur, constitutes the condition of auto-infection. All disturbances in secretion and normal excretion, every arrest or diminution of the respiratory functions, or in the blood-making processes are necessarily followed by the retention of this toxic physiological debris in the body."

So much for the general statement of the doctrine. To proceed now to the special application of it to the pathological processes of pregnancy.

Here again, it is to French authors and investigators that much of our knowledge is owing. Of these, the chief are Bouffe de Saint-Blaise, Pinard, Roger and Claude.

Of the great increase in tissue metabolism that occurs during pregnancy, little need be said. The fact is self-evident and any quantitative estimation is almost impossible. During the nine months of pregnancy, seven pounds weight of animal tissue - the foetus - has to be elaborated. To build this up, the maternal organism has to supply all the materials, and that in a highly elaborated form. It has also to eliminate the waste products of what is/

is practically an endo-parasitic creature, the cellular structure of which is in a state of intense proliferative activity. One may get some idea of the increase necessary on the part of the mother's ingestive and eliminative organs, if we compare the intra-uterine with the extra-uterine life of the child in its early stages. At the age of five months, according to Ashby,(7) an average infant weighs 14lbs 14 ozs. - practically double its weight at birth. We can estimate roughly the amount of the milk taken by the child and the amount of the excreta in that time and so obtain by analogy a mental picture of the increased work imposed on the maternal organs. Over against this, can be set the absence of the usual monthly loss by menstruation. But the quantity of organised material, namely blood, lost even in nine months is small indeed compared to the ultimate weight of the full-term foetus.

As collateral evidence, from the maternal side, of this activity one may cite some observations of Charrin(8) on "Predispositions Morbides de le Periode Puerperale" with special references to Glycosuria and demineralisation. "Le point intéressant de ces recherches" he says "c'est qu'il suffit de faire ingérer 60 à 120 grammes de ce glycose pur, à ces femmes arrivées au terme de leur grossesse pour faire apparaître le phénomène de la glycosurie dite "alimentaire": or à l'état normal, ces mémes femmes pour aboutir/

aboutir a ce meme resultat, sont obligées d'eléver cette dose à 140 ou 180 grammes. Cette constatation prouve que la consommation du sucre dans ces conditions est ralentie. Comme, d'autre part, l'economie produit des quantites de ce sucre, il découle de cette donnée, a titre de consequence fatale, l'accumulation de ce corps, autrement dit l'hyperglycemie." And in the same article, detailing a number of observations on the liver and spleen of pregnant and non-pregnant animals he concludes:-

"Il semble donc, en dépit des variations individuelles, que, dans la grande majorité des faits observés, le fer de la rate diminue sensiblement pendant que les foetus se développent et l'organisme parait subir une déminèralisation consistant dans le passage de proportions variables de fer aux éléments en formation."

In this particular connection it is of importance to recall the fact frequently observed in pregnancy of enlargement, more particularly vascular enlargement, of the thyroid gland. From the clinical contrast between cases of Exophthalmic Goitre and Myxoedema taken into account with the histological alterations in the secreting elements of the gland in these two conditions, it is becoming clear now that increased secretion of the thyroid - hyperthyroidea/

thyroidea - has a causal relation to exalted tissue metabolism, and conversely athyroidea determines "life at low pressure" - such as is seen in the phlegmatic sufferer from Myxoedema and the congenital cretin. The hyperthyroidea of pregnancy, then, is one more token of the heightened activity of the maternal organism during that particular period.

There being then, indisputably, this increase in metabolism and with it, necessarily, an increase in the physiological debris requiring to be eliminated, it is evident that at the moment when the excretory organs as a whole - intestine, kidney, lung, skin - fail to overtake the increased work thrown on them, the physiological processes of pregnancy merge into the pathological.

Puerperal Eclampsia has long been considered the typical, though extreme, instance of "pregnancy-poisoning." Long considered to be a variety of uraemia and due to renal insufficiency, doubt was next raised as to whether the renal symptoms were really the cause or the consequence of the condition, and more recently still, the rôle of the kidney in producing the phenomena has been disputed and the liver credited with being the "fons et origo mali." Elaborating this theory, Pinard has under the term "hépato-toxhémie" described and taught the existence of/

of a specific condition comprehensive enough to include nearly all the abnormal phenomena of pregnancy from sickness, pruritus and glycosuria to oedema, haemorrhages and convulsions. His position summed up by M. Bouffe de Saint Blaise[9] is thus expressed:-

"L'insuffisance hépatique est la cause unique (italics mine.) de quelques phénomènes morbides de la grossesse, mais cette intoxication présente des formes bien différantes suivant que tel ou tel poison domine et suivant que l'organisme intoxiqué fournit un terrain de moindre résistance, par hérédité, maladie antérieure ou disposition morbide quelconque."

My object in the present thesis is not to argue for or to criticise such a theory of a specific toxic condition, for it hardly admits of proof or disproof in the present state of our knowledge, as I wish rather to show from a clinical point of view how the general doctrine of Auto-intoxication serves to explain on a common basis, many of the deviations from the normal which we find during pregnancy, covering at the same time, a wider field than the special lesions and manifestations of "Hepato-Toxaemia."

But Pinard's theory deserves at least more than passing notice and I summarise briefly an account of his argument as detailed by Bouffe de Saint Blaise[10] at the last International Congress of Obstetrics and Gynaecology/

Gynaecology - so far, at any rate, as it deals with the special rôle of the liver in the production of the condition.

While admitting the importance of the kidney in favouring and completing the retention of toxic substances, he maintains that the liver plays the preponderating part either from imperfect action as a secreting organ or from failing to prevent the passage into the general circulation of poisonous substances from the intestine brought to it by way of the portal vascular system.

Cases of Eclampsia are recorded where neither albuminuria nor Bright's disease is present, the frequency of jaundice after eclampsia, the similarity of it to the nervous affections of severe jaundice and the mode of death in fatal cases - these facts he adduces as clinical proofs of his theory. Again, quoting Potocki(Bull. Med. 1898 p.105) to the effect that "l'eclampsie apparaît de préférence chez des femmes dont le rein ne presente pas de lésions anatomiques," he refers to the relative toxicity of the urine and the blood-serum - the latter being increased in the condition and the former subnormal, - and lastly, to the diminished excretion of urea, as experimental proofs of his position. The value of milk diet in averting threatened attacks is adduced - though to the unbiased it would appear to/

to argue as much for the renal hypothesis.

Finally, he holds, that pathological anatomy shows in practically all cases in the liver, "lésions necrobiotiques" whilst the kidney may show all possible variations from absolute integrity, simple congestion or nephritis to haemorrhages and necrosis.

Having followed his argument thus far, we may leave this aspect of the subject for the present, reserving till later the consideration of the clinical features of the condition as described by Pinard in his oral teaching, for he has not himself published or written on the subject.

In turning now to the clinical aspects and applications of the doctrine of Auto-intoxication, I think the following conditions reasonably come within its scope and, so far as I can, I shall illustrate them with cases, taking them in the following order.

I. Anaemia.
II. Chorea.
III. Peripheral Neuritis.
IV. Hyperemesis.
V. Pinard's "Hepato-Toxaemia."
VI. Eclampsia.
VII. Acute Yellow Atrophy of Liver.
VIII. Various minor manifestations.
IX. Mental disorders.

1./

1. Anaemia.

In his well-known text-book, Playfair[11] discarding the old idea of plethora, describes the normal state of the blood in pregnancy as "much more nearly approaching the condition of anaemia - being at the same time, more watery and containing less albumen" than in the non-pregnant state. "Relative anaemia with hydraemia", therefore, is a fair expression of the state existing. That this, however, at times merges into a grave and even fatal anaemia, is illustrated by the two following cases.

Case 1. Mrs R. aet. 31 yrs. iii-para was confined on July 19th 1899. The delivery, both of child and after-birth, was quite uneventful and there was no haemorrhage. She had not been seen for some months previously, and the pallor she presented contrasted forcibly with her former condition. On the day following the confinement, it was elicited that for four months she had been feeling out of sorts, weak, languid, breathless, at times dizzy, subject to attacks of palpitation and very capricious in appetite. There had been no abnormal sickness in early pregnancy, but latterly a marked diminution in the quantity of urine, accompanied by constipation.

She had not sought advice as the condition was thought to be entirely due to pregnancy, and she hoped/

hoped "time would put it all right." On the fourth day after delivery, it was necessary on the account of the persistent debility to review the case thoroughly, and further signs of marked anaemia were evident in the fainting, dyspnoea, headache and debility complained of. Physical examination as follows:-

The pulse was 115 per minute, regular but very compressible, Haemic murmurs heard at each valvular area and in the neck. Respirations 30 per minute, no evident oedema of lungs. Temperature normal, tongue clean but pale, flabby and tooth marked, no enlargement of liver or spleen.

Skin slightly tinged with yellow - paler and more diffused than in the browning of Chloasma, sub-cutaneous fat not diminished, some dropsy of both lower extremities, mucous membranes intensely pale. Urine, about 30 oz. per diem, otherwise normal and free from albumen. The child, as advised, was removed from the breast; the patient placed on strict milk diet with meat juice at intervals and for medicine was given Ammonio-Citrate of Iron with Digitalis. The oedema of legs yielded considerably and the quantity of urine increased. The bowels moved daily with a morning saline aperient. Some slight improvement ensued and on the twelfth day she tried to sit up a little, but fainted and had to give up the attempt. The anaemia showed no improvement/

provement and Fowler's solution was added to the medicine. On August 2nd. she developed partial paralysis of the right side with marked difficulty of speech - both in finding words and in articulation. This passed off in thirty-six hours and was probably due to serous cerebral effusion. On August 4th, the lemon-yellow tingeing of the skin was more marked and sickness set in with the result that both the Digitalis and the Arsenic had to be stopped. Brandy and Soda in sips, ice and a Bismuth and Pepsin mixture partly relieved this, but the general condition was steadily deteriorating. On August 10th, she had a similar cerebral attack to that on the 4th and remained unconscious for four hours. No absolute paralysis was left behind and the paresis gradually improved though her memory remained impaired. On the 14th, the pulse was noted as 130 regular but beginning to be "thready" and "running" and the respirations more rapid and shallow. The expression also was becoming anxious. On the 17th, she lay apathetic for some hours on end, and only roused up for nourishment or stimulant. On the 19th, there was complete unconsciousness with a flickering pulse and Cheyne-Stokes breathing, followed early on the 20th by death.

Case 2. Mrs A. aet. 33 yrs, iv-para, was delivered November 29th 1899. The child was born easily/

easily and the placenta removed manually as there was some threatening of third stage haemorrhage. She was markedly anaemic and has been repeatedly in recent years under treatment for Chlorosis. The pulse, quarter of an hour after delivery, was 102 per minute, irregular in time, fairly full in volume but very low in tension and the heart acting tumultuously. Then, raising her head for a drink, she had a syncopal attack and the pulse became almost imperceptible, but improved again with stimulant. She was on the following day advised to make no attempt to suckle the child. Examination of the heart showed dilatation, evidently due to the anaemia, of the left ventricle - there being increased area of dullness on percussion, displacement outwards and diffusion of the apex - beat, and a loud mitral murmur conducted along the ribs. In addition there were haemic murmurs at the base and a typical venous bruit in the neck. As the cardiac symptoms were urgent, she was given Digitalis, Nux Vomica and Spirit Ammon. Aromat. with stimulant regularly. In a few days she was given also Tabellae of Alginate of Iron. For about three weeks she remained almost at a stand-still - losing no ground though gaining none - having repeated attacks of fainting, dyspnoea and palpitation. Distinct enlargement of the thyroid/

thyroid was noticed at this time. On the 24th day, when the pallor of the mucous membranes seemed to be rather less, she developed phlegmasia of the left leg followed ten days later by phlegmasia in the other. A month after confinement, her appetite and digestion having been fairly well maintained throughout, her colour was better, the pulse regular and stronger and the heart apparently normal in size. The digitalis was now stopped and Ammonio-Citrate of Iron with Arsenic given. At the end of seven weeks she was able to sit up in her bed-room, was on full convalescent diet and was put on to Pil. Ferri regularly. This she took for fully three months subsequently, paying careful attention to the regulation of the bowels by bi-weekly doses of Sulphate of Magnesia. When seen at the end of this time, she was in good health, feeling better and more active than she had done for some years, and with little sign of her former Anaemic condition.

These two cases illustrate two distinct types of Anaemia - the first, steadily progressing to a fatal issue, being of the nature of a Pernicious Anaemia, and the second, a Chloro-Anaemia aggravated by pregnancy. Both conditions are explainable on the hypothesis of Auto-intoxication acting in one of two ways - either by increasing haemolysis or/

or blood-destruction, or secondly, by impeding blood formation.

Oliver[11] records three cases ending fatally of severe Anaemia in pregnancy and quotes Spiegelberg's twenty-five collected cases, nearly all of them fatal.

He suggests, following Bunge's ideas as to the non-absorption of iron from the intestines, that this anaemia is due to the direct transference of haemoglobin from the maternal system to the foetal and that the production of haemoglobin by the mother does not keep pace with the demands of the foetus. That this is the part explanation receives confirmation from Charrin's more recent observations on "Maternal demineralisation" already referred to, but it does not carry us very far.

Clarke's teaching that Chlorosis was due to a foecal intoxication is not so widely accepted now as formerly, more modern views ascribing it, as Gulland[13] does, rather to deficiency of proteid food. The importance, however, of giving saline aperients during a course of iron - not merely to counteract the constipating tendency of most iron salts - is strong clinical evidence of the haemolytic properties of effete products gaining admittance to the general circulation. Again, it is generally accepted that pernicious anaemia is of a definitely/

definitely toxic origin. Hunter's researches on haemolysis[14] have practically decided that point, whether the source of the toxins be from the gastro-intestinal tract, from septic absorption, or systemic poisoning.

The analogy further of the Anaemic conditions occurring in the course of Chronic Bright's disease, in the cachexia of malignant disease, and in Malaria, in all of which toxins are circulating in the blood, is further and convincing evidence that pregnancy itself, if it be accompanied by relatively inadequate elimination of the waste products of Metabolism and in the absence of gross lesions of liver or kidney can, by the accumulation of those waste products, give rise to toxic Anaemia of the gravest nature.

2. Chorea.

The subject of Chorea as a complication of pregnancy seems hardly to have the attention it merits in the text-books of obstetrics. And very little advance in our knowledge of the condition seems to have been made in recent years. Thus I find in an old edition of "Schröder's Midwifery" as full a treatment of the subject as in modern text-books written some forty years later.

The literature has been reviewed recently by Buist/

Buist[15] and a complete and exhaustive critical analysis made of all recorded cases in a valuable paper read by him before the Edinburgh Obstetrical Society.

More recently Dakin[16] has published an interesting account of seven cases observed by him.

A succinct summary of the present state of our knowledge is appended by Stewart[17] to an Encyclopaedia article dealing with Chorea generally. But the subject deserves further study.

Case 3. M. K. aet. 18 yrs, primipara was first seen early in August 1899. She was a servant girl, unmarried, and had been sent home on account of having developed "St. Vitus's Dance" some ten days previously. She was said to be in the seventh month of pregnancy and abdominal examination bore out the mother's statement. The case was obvious in its nature and the irregular movements of the face, arms and legs quite characteristic. Family history on enquiry, gave negative results - rheumatism, chorea, epilepsy and insanity all absent. Personal history of the patient was equally so. She had never had Chorea before - no rheumatism, no "fits" and no history of fright. Her work though fairly hard, had not been excessive, and her general bodily condition was good.

She/

She was not of a hysterical or neurotic disposition, in fact, rather otherwise, and the existence of her illegitimate pregnancy did not seem to trouble her very much.

Careful auscultation failed to detect any cardiac murmur whatever. In short, all the ordinarily accepted causes of Chorea were characterised by their absence.

There being no personal or family proclivity to rheumatism, the case was thought a suitable one for arsenic and on August 12th she was put on Liq. Arsenicalis M.5.t.i.d. after food. Generous diet and fresh air, as far as possible, was advised. On August 20th there was no improvement whatever, and the arsenic was doubled. On the 28th, she was decidedly worse, could hold nothing in her hand, could not keep the tongue protruded and speech was becoming indistinct and the movements of the limbs incessant. The Fowler's solution was increased to 15M - and given in milk. September 6th, signs of saturation with arsenic began to appear in gastric irritability and conjunctivitis and on September 8th, as it appeared to be doing no good whatever, it was stopped. Full doses of Salicylate of Soda with Potass were substituted on the possibility of some undetected rheumatic origin, but made no impression and on September 13th as the case was beginning to look serious/

serious recourse was had to sedatives. Bromide of Potass was given in doses of 25, 35 and 45 grains without doing more than making her a little dazed. Three drachms of Syrup of Chloral were equally ineffective in producing sleep, and 40 grs. of Sulphonal gave her quiet for a couple of hours only by night. She was now entirely confined to bed, and the violence of her movements repeatedly threw her out. Her speech was quite unintelligible and consisted entirely of monosyllabic ejaculations, but she understood what was said to her.

Feeding was accomplished only with the greatest difficulty. The elbows, shoulder blades and sacrum showed excoriations of the skin through the unceasing movement, and the limbs were marked by bruises. On September 25th, after consultation, premature induction was advised but the parents were unwilling as immediate alleviation could not be guaranteed. The last month of pregnancy passed in this aggravated state and by October 20th, the patient was thin and wasted, with eyes sunken and lips baked. Pulse was 130, weak and irregular, respirations 25 and very "jerky". Temperature 100·5. She was still taking stimulant and liquid nourishment fairly well, but in very small quantities by the feeder - in fact, she had been living for three weeks on egg milk and brandy/

brandy "flip." Full doses of bromide and Sulphonal gave her a little rest. Opium (as Nepenthe) seemed useless. On October 23rd labour set in and when first seen the head was already on the perineum and delivery ensued easily three hours later, without assistance or difficulty. The child, though small, appeared healthy, but died suddenly on the third day after being "in statu epileptico" for twenty minutes. The girl's condition improved distinctly after delivery - the vehemence of the movements being markedly diminished. She took nourishment freely and well, and by the end of a fortnight was able to be propped up in a chair. But it was noticed that her mind was considerably affected. Her expression now became vacant and her manner childish. Speech was slow and dragging and her memory impaired. This gradually improved, and by the end of six weeks, she was able to walk outside and seemed nearly better except for a slight "fidgetting."

A fortnight later, she was supposed to have caught cold, and certainly had some catarrhal symptoms, followed abruptly by a severe relapse of Chorea. This for a time was so severe as to necessitate her being in bed again, but improved after persisting three weeks fairly acutely and gradually disappeared a month later. In two months more, being/

being six months after her confinement, she was sufficiently well to obtain a fresh situation, and on recent enquiry, I find she has continued in good health.

I have given this case in considerable detail as it presents many points of interest, but I wish to confine myself here to the question of etiology. The general teaching of the obstetric text-books is that Chorea gravidarum is purely a functional neurosis - an exaggerated nervous reflex from irritation due to the enlargement or the distension of the uterus. Coupled with this, as the peripheral exciting cause, is the heightened irritability of the nerve centres associated almost normally with pregnancy. But here, too, a good case can be made out for a toxaemic origin. As to the causation of Chorea generally, pathological anatomy gives no clue. Various lesions have been described e.g. embolism of the cerebral arterioles, perivascular distension and fibrosis, punctate haemorrhages in the brain, cloudy swelling of the cortical motor cells, but these all are of inconstant occurrence and only found in fatal cases of very acute Chorea and more probably are merely accidental and not causal. The close relation of rheumatism in some form or another, is now generally accepted, and points/

points to a toxic origin - whether it be that Chorea is due directly to a specific rheumatic poison, or, what is more likely, to one of a complex of poisons which results in what we clinically term rheumatism with its various manifestations of articular lesions, endocarditis, tonsillitis, erythema nodosum and subcutaneous nodules.

Again the clinical picture argues strongly in favour of such an origin. The description given by Broadbent[18] is graphic and the analogy he cites an apt one. He terms it "a delirium of the sensori-motor ganglia. In delirium there is loss of control over the mental processes, with rapid succession of incoherent and imperfect ideas; in Chorea loss of control over the motor apparatus with movements excessive in point of number and extent, but wanting in vigour and precision." Now, while wishing to avoid being carried away by mere phraseology, one cannot but admit the term "sensori-motor delirium" to be highly applicable. And, as delirium of the higher centres is practically always of a toxic nature, whether arising from hyperpyrexia, specific poisons, or retained waste products, so we have valid grounds for believing that the motor centres may be similarly affected.

Osler[19] in a monograph on the subject leans to this view and states "Though the disease is usually/

usually regarded as a neurosis, the clinical character of the severer cases has suggested to many recent writers, that it may be due to a specific poison." Further on, he suggests that it should be classified among the infectious diseases.

More recently still, Kauffmann(20) discussing the "Neuroses of Childhood" groups Chorea with migraine, epilepsy, tetany and night-terrors and, while admitting emotional and hereditary factors as elements in their causation, maintains that these are examples of gastro-intestinal intoxication. In a large majority of cases he found habitual excess of food, unsuitable food, catarrh of the intestine or constipation to exist. In many, indican in quantity was found in the urine ("Which is derivable only from the indol in the intestines") and successful treatment by dieting, saline aperients, calomel and intestinal antiseptics is further evidence of the correctness of his hypotheses.

With this mass of clinical evidence, I think it may be validly held that the active causal agent is a toxin, and the other factor - heightened nervous excitability - in the case regarded as merely a predisposing one. In the Chorea of pregnancy then, both these factors have a place, but the toxaemic factor must be recognised as the predominant one, and the time honoured "functional neurosis" theory less emphasised/

phasised. In the case of M.K. which I have recorded, reviewing the case at this distance, I can see much to support Kauffmann's views though it did not strike one at the time. The emotional and rheumatic factors in her case were entirely absent. Drugs given as nerve sedatives were practically futile. But I find she she left a home where food was scanty and of poor quality, for a situation in an inn where abundance reigned. Excessive feeding and gross constipation followed: and pregnancy, with imperfect elimination, completed the amount of toxin production necessary to inhibit the controlling or stimulate the sensori-motor ganglia.

3. Peripheral Neuritis.

The occurrence of peripheral neuritis or poly-neuritis in pregnancy is scarcely referred to in obstetric text-books. But, if rare, it none the less occurs. The most complete modern account with collected cases is given by Turney[21] and two cases were reported by the late Dr George Elder[22] to the Edinburgh Obstetrical Society. As I have not been fortunate enough to meet with an illustrative case, I shall only, briefly, refer to the causal relationships.

Polyneuritis is a typical example of a systemic poisoning affecting the nervous system - whether the exciting cause be alcohol, metallic poisons, or specific/

ific poisons, e.g. those of diphtheria or scarlet fever. The disparity in kind of these poisons suggests rather that the real materies morbi is not the primary poison itself, but some substance, the result of perverted metabolism, which is hindered from elimination by the presence of those specific poisons. This finds corroboration in the extra intensity manifested in case where the exciting cause is found in a combination of poisons as in the epidemic, which with Manchester as a centre has been traced to arsenicated beer. Here we have a combination of a mineral poison with alcohol, either of them a sufficient cause singly, and together acting with unprecedented vigour.

Pregnancy then, with its increased toxicity of serum seems to provide a condition of affairs suitable to the evolution of neuritic affections and now that attention is drawn to the condition, more cases are likely to be described. Many are overlooked, slight or partial cases, being put down as merely reflex in origin or attributed to alcoholism avowed or concealed - as in one case eventually proved to be due to the consumption of eau de cologne.

Many cases are preceded by severe vomiting and it has been suggestedthat this is the actual cause of the neuritis. But it is not of constant occurrence and evidence points rather to community of origin/

origin.

We must exclude, of course, cases after delivery which are obviously of traumatic or septic origin. The use of forceps has at times been followed by neuritis from injury to the intra-pelvic nerves. Septic conditions of a sub-acute or chronic nature at times have this result. But excluding such cases and excluding those others of recognised origin, there still remains a definite group of cases in which pregnancy alone appears to be the exciting cause and explainable only on a theory of self-intoxication. And the relatively rapid recovery of those cases on the termination of pregnancy is in complete accord with such a theory of production.

Post script.

Turney's interpretation of a case described by Lawford Knaggs as "Reflex Amblyopia in pregnancy" is of particular interest in this connection. Abortion was procured and recovery commenced at once. The case was evidently, as Turney says "an example of retro-bulbar neuritis of toxic origin."

4. Hyperemesis.

It is generally held and taught that this grave complication of pregnancy is but an exaggeration/

ation of the emesis that is practically of normal occurrence and which is indeed looked for as evidence of the existence of pregnancy. While it is true clinically, it does not follow that it is so etiologically. Cases certainly are found in all and varying degrees of severity - from those in which vomiting is all but absent to those in which it runs to a fatal issue or in which a fatal issue is only averted by the premature emptying of the uterus. But it does not therefore follow that the causal factors are the same alike in slight cases and in severe. There is probably a difference in kind as well as in degree.

To bring this point out, it will be necessary to consider some of the theories advanced to explain the mild or physiological vomitus gravidarum. The explanation generally accepted is that it is due to a simple reflex act. The act of vomiting is controlled by a special centre in the floor of the medulla oblongata which co-ordinates the various groups of muscles involved. This centre is stimulated by impulses variously originated.

Evans(23) advancing a new theory of the origin of those stimuli summarises previous suggestions thus:-

"Mechanical pressure of the enlarging uterus on the nerves of the pelvic ganglion: stretching of the muscle/

muscle fibres of the uterus causing pressure on the nerve endings: versions and flexions of the pregnant organ: ovarian irritation from uterine pressure: diseased conditions as Endometritis, cellulitis, endocervicitis etc. have all been advanced as factors in the production of this irritation."

In this list there is certainly ample scope for choice. But mere mechanical causes are inadequate, and local pathological states inadmissible, to explain what is so obviously of universal and normal occurrence.

Evans, himself, advances the theory that the reflex is due to the rythmical contractions of the uterus which persist during pregnancy and cites the occurrence of vomiting in renal, appendicular and hepatic colic as analogous instances. Morning sickness, he explains, as due partly to increased irritability of the nerve centres from accumulation of effete material and partly to more energetic uterine contraction from engorgement of the pelvic circulation the result of assuming the erect posture.

This fails, however, to explain why it should cease after the fourth month. In fact, the logical conclusion of such a theory would be that the "vomitus" should continue with increasing severity to the end of pregnancy. But it raises the question of how far waste products or toxins are responsible.

It/

It is of course evident that the centre in the medulla may be directly stimulated by agencies brought thither by the circulation, just as the respiratory centre may be affected. Some hold, as Dirmoser, (quoted by Evans from an article in the Wiener. Med. Wochenschrift Aug. 1897) that the entire phenomena are due to intoxication. But this theory also, is open at the outset to objections. It implies the presence of a pathological condition of almost universal occurrence: moreover, it fails as does the simple reflex theory to explain why vomiting should usually cease about the fifth month, and why it is usually worse in the mornings.

A complete theory must explain at least, the clinical facts of -

1. Morning exacerbations.
2. Cessation usually at fifth month.
3. Occasional persistence as "hyperemesis."

To me it seems that a combination of both factors taken into consideration with the well-known fact regarding the cerebral circulation during sleep (viz. that the brain is anaemic) most adequately covers the ground.

Stated formally, it might be expressed thus:-

First. Vomitus gravidarum is due to irritation of the vomiting centre by stimuli from the pregnant/

pregnant uterus, the actual mode of production of those stimuli being still undetermined.

Second. Morning exacerbations are due to the fact of the brain cells being in a state of greater irritability owing to the tissues having been anaemic during the hours of sleep.

Third. It disappears usually after the fourth month as the enlarging uterus permits of less blood being in the abdominal veins and so more venous blood in the cerebral system by night.

Fourth. Exceptional cases occur where, from the presence of waste products in the circulation, due to imperfect elimination or perverted metabolism, the vomiting centre is stimulated directly and the sickness is excessive either in severity or duration.

I am not aware of the fact of cerebral anaemia being adduced in part explanation of the phenomena hitherto. But it is a known fact, and in keeping with it is the observation frequently made that a hot drink before rising frequently checks the sickness. This evidently acts indirectly by stimulating the circulation and sending to the brain tissues a copious/

copious supply of arterial blood. In favour of proposition three is the clinical fact of the sleeplessness and restlessness so often noted in the later months of pregnancy. The brain does not become so thoroughly anaemic in sleep as in the non-pregnant state. Or, alternatively, it may be argued that this venous excess in the later months has a sedative effect on the Medullary centres.

This theory has the advantage of invoking pathological states - auto-intoxication - to explain only abnormal cases as in proposition four.

Bearing on this, I can recall two cases, one multiparous (where the vomiting persisted till the seventh month severely), the other primiparous (where the vomiting was very acute, through the entire day in the early months) in which bismuth, oxalate of cerium, alkalis, stomachics, bitters, nux vomica and ice all failed to do any good but in which a saline aperient used regularly resulted in marked benefit, assisted by an occasional mercurial pill. Cases of hyperemesis are always anxious and often end disastrously. Their early recognition and treatment as auto-intoxications by judicious eliminative treatment seems likely to produce better results than our present methods do. And the doctrine affords a good working hypothesis for an improved therapeutic.

5. Hepato-Toxaemia.

The/

The existence of this condition and its detailed description by Pinard have been already referred to in this thesis (vide p.11.) together with the arguments adduced in favour of its being the intoxication par excellence of pregnancy. Clinically numerous cases have been described in past years as eclampsias, actual or impending. One case has been well described from the present point of view by Fothergill and Stenhouse[24] and Fothergill in an appendix to the second edition of his textbook gives a systematic description of the condition.

Kynoch[25] also has described a series of cases. The clinical manifestations summarised are "headache, sickness, salivation, some jaundice, albuminuria, chloasma, pruritus, herpes, neuralgia and neuritis. Severe cases may end in acute atrophy of liver or in eclampsia." Examined critically, the theory seems to attempt too much. It concludes practically all abnormal accompanimnets of pregnancy other than those of s specific or local origin.

It attributes to liver-insufficiency all that has hitherto been attributed to impaired kidney function and to perverted tissue metabolism generally. That some cases of this nature do occur is indisputable. That the theory is so all-embracing is controvertible. For in the male and non-pregnant female, we find numerous cases of liver insufficiency/

sufficiency unaccompanied by all this train of symptoms. Again, there is no evidence that pregnancy puts any prepondering strain on the liver as an eliminating organ - more than on other excretory organs. Further, the close analogy of uraemia to the group of symptoms described seems to argue strongly for the older view that renal insufficiency is the determining factor in the condition - whether the kidney is the primary cause or whether, as seems more likely, direct renal symptoms are secondary only to abnormal tissue changes and, when established, precipitate the phenomena of intoxication by a vicious circle of cause and effect.

Unless we find clinically, some alteration in size or tenderness of the liver, some jaundice, altered motions, glycosuria or bilious urine, together with signs of intoxication, we are not justified in attributing to the liver the causa causans of the condition.

With these reservations, we must be prepared to recognise the occasional occurrence of intoxication of an hepatic origin, and I think the following an instance of it.

Case 4.

Mrs A. iii-para, four months pregnant was seen first/

first on account of excessive swelling of the legs and piles. There had been undue sickness, persistent headache, foul coated tongue and constipation. She was known to be somewhat alcoholic. Urine was scanty and loaded with urates but free from sugar and albumen. At five and a half months, distinct enlargement of the liver was noted. It projected 1½" below the costal margin, was smooth to the touch and very tender. The case was then looked upon as one of pre-cirrhotic enlargement and while the advisability of inducing abortion was being mooted, the uterus emptied itself spontaneously and all symptoms rapidly subsided. Rest, milk diet and diuretics were tried in the early stages with very slight benefit. Looking back on the case, now, I feel that cholagogues and saline aperients would have been productive of more advantage.

One suggestion from this case is that habitual abortion in non-syphilitic subjects may be due to this condition of Hepato-toxaemia. I have noted in practice two patients, to my knowledge non-syphilitic, one of whom has had four successive abortions and the other five, who are subject to severe fortnightly "bilious attacks" and who suffer in excess from the various minor ailments of pregnancy - headache, sickness, neuralgia, and signs almost of a gouty nature/

nature - until pregnancy terminates spontaneously at or about mid-term.

Another case of this type is the following.

Case 5. Mrs B. aet. 24 i-para. Confined at full term July 17th 1899 - labour easy and uneventful. Twelve hours after delivery patient had a severe convulsion and was in deep coma when seen. The case was diagnosed as an eclampsia at the time, though the urine contained no albumen, and there was no dropsy whatever. The urine was not diminished in amount, but contained bile and was loaded with urates. She had never had any fits previously. She had been subject to frequent "bilious attacks", but these had abated in the later months of pregnancy. At the time of confinement, there was no obvious jaundice, but some tenderness over the liver. Routine treatment as for eclampsia was adopted - chloroform, chloral, bromide of potass, calomel in repeated small doses, and vapour baths. She had eight convulsive seizures during the first thirty-six hours being in a stupor between the attacks, from which, however, she could be partly aroused. Improvement seemed to begin after the passage of several bilious motions.

The patient ultimately recovered, but remained in a weak and languid state for several weeks.

On November 19th 1900, she was delivered of an eight/

eight months child. Twelve hours after delivery she had a convulsive attack and had three similar seizures on the second day of puerperium. After each seizure she was profoundly unconscious with both pupillary and conjunctival reflex gone. Urine was again found free from albumen, and dropsy absent. She had a crisis of copious biliary vomiting and again improved rapidly after several bilious motions due to repeated small doses of Sulphate of Magnesia. The whole attack resembled closely the previous one but was much less severe.

In these cases, then, the kidney never came under suspicion as the urine was almost normal in quantity, free from albumen and from casts.

The last case was at the time certainly looked on as an eclampsia of the less common type, but looking back on it now, the prominence of liver symptoms leads me to have no hesitation in putting it down to "Hepato-Toxaemia."

To sum up - liver-insufficiency in pregnancy can cause auto-intoxication. There is a train of symptoms such as are common to toxaemias of different origin, plus a few of definite hepatic origin. But while eclamptic conditions may occur, eclampsia of a renal kind is more common. And the claim for "Hepato-Toxaemia" as explaining <u>all</u> toxaemic conditions of pregnancy is contrary to clinical experience.

The probability of the occurrence of mixed cases must/

must be borne in mind.

6. Eclampsia.

Eclampsia shares with placenta praevia the position of being the most alarming complication of pregnancy and parturition. As to its causation there is no need to refer to the older hypotheses - the Traube-Rosenstein theory, the germ-theory, Riviere's theory and so forth. It is now so generally accepted as being the climax of a process of self-intoxication that the argument need not be detailed here. At one time, this was thought to be of renal origin, pure and simple, and to be essentially identical with Uraemia - or intoxication from retained urinary products. But it is now held to be of a more general origin - due to perverted metabolism or defective elimination of waste products generally, and not to disease of one particular organ primarily at fault.

As Davis puts it, quoting Merletti(26) "while urea itself is not a poison, but represents the finished product of metabolism, it is incomplete urea in the blood in the form of toxines which causes eclampsia."

The term has certainly been loosely applied in time past - being used almost as synonymous with puerperal convulsions.

But/

But apopleptic, paralytic, reflex and hysterical conditions can be sifted out. Some cases again no doubt, are of a true uraemic nature, depending on actual and coincident kidney disease. Again reference has been made in the preceding section to the role of the liver in producing such phenomena and the value of "Hepato-Toxaemia" chiefly lies, I think, in separating out a definite group of cases formerly described as Eclampsias. As time goes on, further groups may be distinguished as having a definite origin. Thus it is possible some of these intoxications may be proved to depend on alterations in the thyroid gland in the direction either of excess or defeat. The last stages of a fatal case of Exophthalmic goitre I witnessed resembled in many ways fatal cases of renal eclampsia.

I collected at one time a large number of recorded cases from the Medical journals but found that in clinical history and in treatment those reports so closely followed established text-book descriptions that little fresh was to be learned from them. Accordingly these have been discarded.

I shall therefore only note - and that in tabular form, to save time and space - such cases as I have had under immediate observation and then proceed to consider the practical bearing that Bouchard's teaching and the doctrine of auto-intoxication have on the treatment of the condition.

ECLAMPSIA -- TABLE OF CASES.

. in rder	Name	Age	Pregnancy	Date of Delivery	Time of Incidence	Convulsions	Degree	Treatment	Result.	
									Mother	Child
se 5.	Mrs A.	43	V-para	Nov.29. 94	Eighth Month	Before & After Delivery.	Severe	Rapid Dil. & Routine	Recovered	Recovered.
" 6.	M.R.	21	I-para	Jan. 7. 95	Seventh Month	Before & After	Mod. Severe	Rapid Dil. & Routine	Recovered	Recovered.
" 7.	Mrs C.	21	I-para	Jan.18. 95	Full Term	Before & After	Very Severe	Forceps & Routine	Died	Recovered.
" 8.	Mrs R.	23	I-para	Sep.16. 95	Full Term	Before only	Not Severe	Forceps & Opium	Recovered	Recovered.
" 9.	Mrs G.	38	IV-para	July 21.97	Full Term	Before only	Not Severe	Routine	Recovered	Recovered.
" 10.	K.F.	17	I-para	Oct. 6. 97	Full Term	Before & After	Very Severe	Routine	Died	Died.
" 11.	Mrs F.	22	I-para	Apr.15. 98	Full Term	Before & After	Severe	Routine & Forceps	Recovered	Died.
" 12.	Mrs T.	17	I-para	May 26. 99	Full Term.	After only	Very Severe	Routine & Pilocarpin.	Died	Recovered.
" 13.	Mrs B.	23	I-para	July 17.99	Full Term.	After only	Not Severe	Routine.	Recovered	Recovered.
" 14.	Mrs B.	25	I-para	Nov.18. 99	Eighth Month.	Before & After (prolonged coma)	Not Severe.	Routine	Recovered	Recovered.

The first three of these cases were seen in the Royal Maternity Hospital and are reported in some detail in the report for the winter quarter 1894-95 read before the Obstetrical Society. The other cases were seen in the course of ordinary practice. By "routine treatment", I mean the usual methods adopted in such cases in the Hospital at that time - Chloroform, Chloral, Bromide of Potass, Croton and Vapour baths and early termination of labour.

The table shows the usual preponderance of primiparae, especially young primiparae. Two of the cases, indeed, occurred in young girls of 17 yrs - both fatal. Case 10 was made more difficult by being, obstetrically, an impacted breech case. In case 12 a hypodermic of pilocarpine was given and I have no doubt precipitated the fatal issue by hastening pulmonary congestion.

In two of the hospital cases, induction was done by using Barnes' Bags, and in the remainder of the cases, delivery was expedited by the early use of forceps - two cases alone excepted in which the attacks were not severe, numerous or accompanied by prolonged coma.

Treatment, broadly speaking, is along two lines, first, controlling, second, eliminant. The first, which has in view the prevention of formation of waste/

waste products, implies the use of the sedatives, Chloroform, Chloral, Bromide of Potass, Morphia and Veratrum Viride. Of this last, I have no experience. Morphia is advocated largely by the Rotunda School. Its true place is probably to be used in conjunction with Chloroform to prolong the effects of the latter and diminish the quantity required for control purposes. As to the bromide salt used, Bouchard's experiments conclusively prove that potass is a very definite element in the production of the intoxication and that soda is "40 times less toxic than Potass." It seems therefore, only logical that Sodium Bromide should be exclusively used in such circumstances and administered in full doses per rectum, if it cannot be given by the month.

The emptying of the uterus by the early use of forceps, by turning, or if needed, induction of labour, comes under this heading also. The advisability of such a proceeding is often questioned, but to us of the Edinburgh School it seems only a logical deduction from the hypothesis of toxaemia that the active factor in the production of these toxines, the foetus, should in all, except non-urgent cases, be removed early.

It is in regard to the second heading, that of eliminant treatment, that Bouchard's[27] work is most suggestive.

The/

The channels of elimination available are the kidney, the bowel and the skin. Again, the floating poisons may be diluted by saline injections or may be directly removed by bleeding. As to the relative value of these, Bouchard is very emphatic. Thus he says, "A bleeding of 32 grammes is the equivalent (i.e. so far as removal of toxines is concerned) of 280 grammes of diarrhoeic motions and equivalent to 100 litres of sweat." This casts grave doubts on the value of treatment by hot air, vapour baths and jaborandi. "They remove water indeed, but not the effete matters." It is possible too, that the removal of fluid thus by the skin merely serves to concentrate the poisons in the blood and perhaps but aggravates the condition. This position seems heterodox, but has definite experimental foundation. It brings forward, also, prominently the value of bleeding. At one time used almost exclusively, it has fallen into undeserved disuse. In a curious American book on eclampsia, edited by Michener[28] recording "all the cases which have occurred during the present century within a radius of several miles around Avondale, Chester Co. Penn" - a large proportion of successes are claimed for bleeding as routine treatment. And in my own cases (Case 7 in table) a very definite improvement followed on allowing free/

free haemorrhage during the third stage. In several of Michener's cases, 60 and even 80 ounces were removed with good results, and it is in accord with Bouchard's statement that for getting rid of waste products "bleeding is the best for acute cases and is second only to free diuresis."

To encourage free action of the kidney, Bouchard suggests copious cold enemata "to drive the venous blood of the portal system into the general circulation." This has not been done much in the treatment of eclampsias, but the idea is worth following out. But the method of injection into the cellular tissues of saline solution with Sodium Acetate has in Jardine's[29] hands been unusually successful. This is a happy combination of treatment by "dilution of poison" and by "diuretic action." Bouchard, himself, suggests the use of urea hypodermically, but I cannot find any puerperal case in which it has been so used for diuretic effect. He himself records a pure uraemic case where it produced 7 litres of urine in 24 hours.

To produce elimination by the bowels, croton is frequently employed on account of the facility of administration and rapidity of action. Small repeated doses of calomel would be equally convenient in unconscious cases and act beneficially as anti-

septic and cholagogue. Of course, where the patient can be roused to swallow, repeated doses of salines should be given to clear out all effete matter from the bowel.

In cases where coma is marked and convulsions not so frequent, the use of oxygen seems indicated to facilitate the combustion or oxygenation of the waste products and so directly lessen their toxic effect and indirectly facilitate their removal.

In these various ways then, the theory of toxaemia, specially developed by Bouchard in reference to uraemia, is of value applied to eclamptic conditions in pregnancy.- as criticising certain methods of treatment now adopted, as approving others and suggesting one or two more as worthy of trial.

7. Acute Yellow Atrophy of Liver.

Reference has already been made to this condition as possibly, according to Pinard, being the extreme form of degenerative change associated with Hepato-Toxaemia. But the rarity of the disease, its almost invariably fatal course, the rapidity with which it progresses and the extreme tissue disintegration found post-mortem, seem to mark it off as an entirely separate entity from the group of phenomena following on simple "insuffisance hepatique."

The condition is difficult to define either from/

from a clinical or a pathological stand-point. In severe and fatal cases, the necrosis of the liver cells is almost complete. Thus Coats[30] writes "the tissue under the microscope is hardly recognisable as that of the liver. There are no proper hepatic cells but instead, irregular masses containing fat drops and granular debris, with here and there rhombic crystals of a reddish brown colour. Sometimes Leucine ------ and acicular crystals of Tyrosine are also found." Such rapid and intense cell degeneration can only be caused by a virulent cell poison. It is obvious that two sources of invasion are possible, viz. from the intestine through the portal vein or from the systemic area via the hepatic artery.

Stroebe (Ziegler's Beitrage vol. xxi p.379) quoted by Muir[31] "thinks that it may be of different nature in different cases, that in some it is really of the nature of an intoxication whilst in others the necrosis is associated with the presence of bacteria" and records a case where enormous numbers of bacillus coli were found. But the fact of its occurrence in phosphorous poisoning proves that it is not necessarily organismal.

Whatever then, may be primarily the"fons et origo mali" the condition once established causes clinically/

clinically violent intoxication and Bouchard's references to biliary poisoning(32) help to bring vividly before us and also to explain the special severity of the condition. Thus, he says, "Bile is nine times as poisonous as urine, 4 to 6 c.c. being sufficient to kill in convulsions, 1 kilo. of animal. A man forms in 8 hours enough to kill himself, whereas it needs the urine of 2½ days to do this." If, then, through cellular degeneration, this amount of toxic material (or its precursors in the blood) is uneliminated, we have at once the explanation of the extreme fatality of the condition.

As I have unfortunately, met with no case which I might record, I must be content with insisting on these two points, first, its existence as a distinct process quite apart from insufficiency per se and second, the value of Bouchard's experimental work and his theory of Auto-intoxication as explaining some of the peculiar features of the disease.

8. Various Minor Manifestations.

In addition to the grosser manifestations of self-poisoning, there are many of a lesser degree of severity which nevertheless constitute troublesome accompaniments of pregnancy. For convenience these may be grouped according to systems.

Alimentary System. Salivation has been referred/

red to (page 4) as being produced by one factor of the urinary intoxicants. Constipation has been attributed to it, but more likely in pregnancy is of a mechanical origin. Diarrhoea, certainly, we know as a frequent accompaniment of ptomaine poisoning and it occurs normally in Bright's disease, so we can claim its occurrence in pregnancy as due to intoxication in the absence of other definite causes. But in both these last instances it is probably salutary rather than otherwise and does not call for interference. Stomatitis and pharyngitis I have seen persist during the later months of pregnancy.

Case 15. Mrs B. iii-para, seen in July 1900, seven months pregnant; the mucous membrane of mouth intensely congested and the epithelium peeling off in flakes from the lining of the cheeks and lips. Antiseptic, soothing and astringent mouth-washes with Stomachics were tried but apparently did no good. The condition disappeared spontaneously on the termination at full-term of pregnancy. Similarly, Case 16. Mrs C. v-para, seen May 1900, when eight months pregnant with diffuse catarrhal and granular pharyngitis. Routine treatment gave some relief but not a real cure and the condition only disappeared completely a week subsequent to delivery.

Respiratory System. Asthmatic conditions are liable/

liable to be aggravated and this is apparently due to an intoxicant action and is to be distinguished sharply from dyspnoea due to mere mechanical action. Bronchitic attacks are at times more obstinate in the pregnant patient than otherwise, and this, I think, is directly comparable to "Gouty Bronchitis."

Circulatory System. The abnormalities of this in pregnancy are almost entirely of a mechanical origin, e.g. varix, but purely functional disturbances, such as tachy-cardia and brady-cardia, morbid flushings and some syncopal attacks are probably produced by conditions of auto-intoxication.

Renal System. Albuminuria, oedema without albuminuria and glycosuria occurring in pregnancy all point to errors in tissue metabolism, and are danger signals giving warning of the possible onset of more grave conditions.

Cutaneous System. Urticaria is a frequent concomitant of intestinal intoxication and occurs at times in pregnancy without any other obvious cause. More common is pruritus, not the local form, (where irritating vaginal secretions are chiefly responsible), but generally - the "Prurit generalisé de Stolz"(33) Chloasma, Herpes Gestationis and bronzing are all probably to be explained on the present hypothesis.

Nervous System. Excluding mental disorders which/

which will be referred to later, one finds numerous functional conditions to have their origin in a process of self-intoxication. Thus the vertigo, frontal headache, toothache and neuralgias so often found among gravid women are undoubtedly of this nature. So too, sleeplessness, impaired vision and somnolence at times are met with, especially the first mentioned.

It is these minor conditions that constitute, in the vast majority of cases, the lesser disabilities of pregnancy. As practitioners, we are too apt to think they are normal or almost normal accompaniments of the condition, and to put our patients off with some temporising platitude. These minor phenomena , however, should rather remind us of the graver possibilities they presage and stimulate us to endeavour to secure that our patients walk in the paths of physiological righteousness and in the period of pregnancy, above all others, practice the strictest of personal hygiene. Should this prove inadequate, the case becomes one for assistance by artificial eliminants or full therapeutic treatment.

9. Mental Disorders.

The doctrine of intoxication has found very special application in diseases of the nervous system and more particularly to those of the higher

or/

or intellectual centres. It is, in short, the necessary pathological complement to the modern conception of the trophic and genetic independence of every nervous unit or "neuron."

Further, we must recognise the selective action of different poisons. As Mott[34] puts it "If nitrogenous waste products accumulate in the blood from either defective elimination or excessive production, a toxic environment of the neuron supervenes. But although the toxic substances circulating in the blood must come into contact with all the neurons equally, yet we find that in a great number of instances particular groups, systems and communities of neurons, subserving special functions are especially and, indeed, not infrequently solely affected by particular poisons." Thus, while the poisons of tetanus, alcohol, syphilis etc. affect sensori-motor groups, those of the acute specific fevers, of gout (as seen in aberrant cerebral cases) of diabetes and of uraemia affect the higher centres and are manifested by e.g. drowsiness, delirium or mental aberrations, either temporary or of some degree of permanance.

Puerperal insanity is undoubtedly of this nature and as Duckworth[35] in an address before the Medico-Psychological Society says "while one half of the cases/

cases occur in women of neurotic or insane proclivity, toxic influences naturally affect them more readily and with greater gravity."

In illustration of this toxaemic perversion of the mental functions is the case following:-

Case 17. Mrs A. (referred to previously in case 5 - eclampsia) after artificial emptying of the uterus for eclampsia at the eighth month, in the in-patient department of the Royal Maternity, was restless all night and in the following morning was wildly maniacal, singing, shouting, screaming incessantly, struggling to be out of bed, resisting all control, refusing food and utterly irresponsible. After twenty-four hours this excitation passed off and she made a good recovery.

In this case, then, the process of self-poisoning which produced the train of symptoms, grouped together as "Eclampsia" culminated in intense though temporary intoxication of the higher centres.

In this case, too, it is worth while noticing the marked progressive diminution of the albuminuria after delivery.

Thus: 1. On admission. 4 grammes per litre.
2. Morning after delivery. 2 do. do.
3. Night " " ½ do. do.
4. Second Morning " " Trace.
5. Second Night " " Faint-trace.

(Taken from Maternity Report for winter quarter 1894-95).

But/

But while auto-intoxication explains most cases of insanity during pregnancy, it is important to distinguish the etiological factors in insanity post-partum. I exclude at the outset lactational insanity as probably in most cases due to physical inability to stand the exhausting strain of suckling.

During the process of involution of the uterus a large amount of waste material must necessarily enter the circulation. The uterus diminishes in weight from 22 ounces after delivery to about 6 ounces at the end of the third week. The theories regarding the mechanism of this reduction do not concern us here. But the point is that this large amount of physiological debris has to be eliminated and exists in solution for a time in the general circulation. It would seem, then, that certain cases, though successful in more or less complete elimination during pregnancy, fail during the puerperium to overtake this increased strain, and so intoxication results.

Hitherto a considerable number of cases of puerperal insanity have been recognised as of a toxaemic nature, due to puerperal fever in some form - absorption from the interior of the uterus of decomposing clot or placental fragments; sapraemic conditions of an organismal cause, or true septicaemia - but these toxaemias are essentially ab externo. It has/

has been scarcely recognised that the essentially physiological process of uterine involution can by a process of autò-intoxication, endogenetically, as opposed to organismal or exogenetic intoxication, produce those phenomena. During the year 1900, I had under observation three cases of puerperal insanity which I record briefly, as they seem to have distinct etiologies.

Case 18. Mrs W. xii-para, confined March 12th labour easy and uneventful. Ten days after, she began to have delusions, to be personally untidy, to refuse food. Pulse rate was slightly increased, temperature about normal. The lochia had all along been normal and careful examination excluded septic or cellulitic mischief. As she got progressively worse, and could not be nursed at home, she was removed ten days later to the North Riding Asylum from which she returned four months later perfectly well.

Case 19. Mrs L. vi-para confined March 26th, interference being necessary on account of a marginal placenta praevia. Six days after delivery, she developed delusional and religious mania. Pulse rate about 115. Temperature from 101·5° to 103°. Lochia not foetid but scanty. Vaginal douches of Condy's fluid and intra-uterine douches of chinosol were used repeatedly but brought away nothing.

There/

There was a recent split in the cervix and some effusion in one lateral fornix. The mental aberrancy persisted some five weeks and gradually disappeared.

Case 20. Mrs S. iii-para, delivered June 23rd. Labour easy and rapid and no vaginal examination was made. On the eighth day, she became restless, with rise of temperature and had a slight rigor. The lochia had disappeared abruptly and as septic trouble was feared, an intra-uterine douche was given at once. This brought away a small foul swelling decomposing clot which had been retained. Thereafter, pulse and temperature settled down, but the mental condition deteriorated and after three days of wild excitement, she passed into a state of profound apathetic melancholia. In this state she remained some six weeks and then gradually recovered.

Though I have set down all three cases, I look on the first alone as a true example of auto-intoxication. Careful examination failed to disclose any septic or inflammatory mischief and in their absence the involuting uterus was apparently the source of the toxines. In the other two cases, there was toxic absorption certainly, but it was of an exogenetic nature and in all probability organismal.

A record of cases of puerperal insanity from this point of view might be of some considerable value/

value as regards the form of aberration assumed and as regards the question of prognosis.

This concludes the clinical record of my own cases in which I consider the doctrine of auto-intoxication to be applicable. It is evident at the outset that our knowledge of the subject is as yet in a very vague and theoretical state. We know little of the actual toxines or waste products, as regards this essential nature, though numbers have been isolated and studied chemically - such as creatin, sarcolatic acid and the ammonio-compounds. But the hypothesis is of very real and very practical value.

As Ewald(36) puts it "Aus alledem sehen wir also, dass die thatsachlichen Unterlagen, auf denen die Lehre von der Auto-intoxication beruht, ausserordentlich gering sind, nichtsdestoweniger drangt die klinische Erfahrung in zahlreichen Beobachtungen sehr verschiedenartiger krankheitzustande fast unabweisbar auf die Annahme einer Selbsvergiftung des organismus hin." And if this be true of morbid processes generally, it is especially so of deficient elimination in pregnancy.

The theory is of value as a wide generalisation, explaining a morbid process although in any individual instance it may not be able to specify the particular poison or the appropriate antidote. It provides/

provides a rational basis on which to build a therapeutic applicable to a large number of disorders, major and minor, of pregnancy. And it seems likely that its applicability will be extended as time goes on to other conditions as yet obscure.

It would be out of place here to attempt to detail a complete hygiene of pregnancy and equally so to refer to the details of treatment of the various conditions alluded to and illustrated above. But the practical bearings of the doctrine demand in conclusion some brief consideration. And I think the following are of importance.

First of all, the insidious nature, and the far reaching effects of the process demand its recognition at the earliest possible occasion. This involves the close supervision of the pregnant female. To aid this in actual practice our patients should be encouraged to come and report early in pregnancy - say at the fourth or fifth month - and not defer "engaging" the practitioner till much later on. The careful examination of the urine should become more of a routine and not reserved merely for cases already showing definite manifestations of disease. This examination of urine too, wants to be made more exhaustive. It is not sufficient merely to determine the presence or absence of albumen. It has been shown that the quantity of toxines present in the/

the serum and in the urine varies with the amount of urea excreted. A fall in the urea-excretion signifies the retention in the blood of waste products that ought to be eliminated and this reduction is the earliest token of impending danger. Albuminuria follows later and is a definite danger signal and calls for active investigation and treatment.

Another valuable lesson is the importance of securing thorough oxygenation. And this raises the whole question of fresh air and exercise during the pregnant state. It has been definitely shown that it is the non-oxidised and unreduced waste products of metabolism which are the most noxious and that the least injurious is urea itself - which is the final product, the finished article as it were, of the human laboratory.

It is our duty to enforce on our patients, the paramount necessity of caring for their bodies, but in a methodical manner and not by mere spasmodic efforts. The combustion processes must be carried on with regularity as well as with vigour. Yet all exercise must be indulged in short of actual fatigue.

Over-indulgence means excessive productions of waste products and therefore a source of definite danger. In this relation, then, the practitioner may be called on to decide if a patient may cycle or ride or take part in games, tennis or golf, in the early/

early months of pregnancy, or again later it may be necessary to restrict her to simple walking or carriage exercise.

But above all, does the doctrine of Auto-intoxication emphasise the value of thorough elimination and the importance of having the excretory organs in an active state. And should any one of them fail, the value of compensatory or vicarious secretion has to be borne in mind.

In actual practice, we know that a very large proportion of women are habitually careless as to the emptying of the bowel. In pregnancy this carelessness is often aggravated. Practitioners, too, apparently, as a matter of tradition, refrain from advising aperients during pregnancy fromaa fear of inducing abortion. But while drastic purgatives are distinctly contra-indicated, reasonably moderate doses of any of the saline aperients cannot but do good, emptying the bowel, stimulating the liver, relieving portal congestions, clearing away headaches and generally improving the tone both of body and mind. If there is gross constipation enemata are called for, and if evidence of hepatic insufficiency then calomel in some form can be employed.

As regards the kidney - any evidence of renal inadequacy calls for interference whether it be quantitative merely or qualitative. The diet should be/

be regulated so as to contain the minimum of nitrogenous matter, and in severe cases should consist almost exclusively of milk. The system should be flushed out with copious supplies of potable water and medicinal diuretics given - avoiding, as Bouchard insists, the salts of potash.

Finally, as regards the hygiene of the skin, the importance of warm and loose clothing, the necessity of regular bathing and the value of occasional turkish baths have to be borne in mind. If signs of toxaemia set in, the importance of stimulating the sudoriparous glands by diaphoretics, by vapour baths or the hot wet pack are the definite indications of the theory. The value of bleeding has been already referred to.

Such are the ideas suggested by the doctrine of Auto-intoxication as applied to the hygiene and to the therapeutics of pregnancy. The actual practical details may be elaborated indefinitely according to the particular manifestations of the individual case. But the value of the theory lies in the broad general principles suggested. And the appreciation of these principles cannot but be helpful in systematising treatment.

Finally, should, in any well-marked cases of puerperal toxaemia, energetic treatment along these lines, fail to produce definite improvement after a fair trial, the case must be reviewed to determine the/

the propriety of terminating the pregnancy. If the toxines cannot be eliminated from the maternal system by ordinary methods then the source of the toxines - the ovum - must be removed and that before the condition has advanced far enough to menace the mother's life. The ultimate results and danger of puerperal toxaemia are well enough known, now, clinically, to justify and warrant the extreme precedure of early induction of labour.

Knowledge has been in all time, in a state of evolution and developement. Ours is essentially a progressive science. And in this particular field, though the foundations have been laid and the structure dimly outlined, yet much remains to be done, alike by the practitioner by the bed-side, and the chemist and the physiologist in the laboratory. And the investigation is likely to be fruitful of results. "Möge es dem neuen Jahrhundert beschieden seinuns auch hier eine bessere Einsicht zu bringen" (Ewald).

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